Real-Time Three-Dimensional Echocardiography for Measurement of Left Ventricular Volumes

Michael A. Schmidt, MD, Chikai J. Ohazama, PhD, Kwabena O. Agyeman, MD, Raisa Z. Freidlin, MS, Michael Jones, MD, Joy M. Laurienzo, RN, Cynthia L. Brenneman, RN, Andrew E. Arai, MD, Olaf T. von Ramm, PhD, and Julio A. Panza, MD

Left ventricular (LV) volumes are important prognostic indexes in patients with heart disease. Although several methods can evaluate LV volumes, most have important intrinsic limitations. Real-time 3-dimensional echocardiography (RT3D echo) is a novel technique capable of instantaneous acquisition of volumetric images. The purpose of this study was to validate LV volume calculations with RT3D echo and to determine their usefulness in cardiac patients. To this end, 4 normal subjects and 21 cardiac patients underwent magnetic resonance imaging (MRI) and RT3D echo on the same day. A strong correlation was found between LV volumes calculated with MRI and with RT3D echo ($r = 0.91$; $y = 20.1 + 0.71x$; SEE 28 ml). LV volumes obtained with MRI were greater than those obtained with RT3D echo (126 ± 83 vs 110 ± 65 ml; $p = 0.002$), probably due to the fact that heart rate during MRI acquisition was lower than that during RT3D echo examination (62 ± 11 vs 79 ± 16 beats/min; $p = 0.0001$). Analysis of intra- and interobserver variability showed strong indexes of agreement in the measurement of LV volumes with RT3D echo. Thus, LV volume measurements with RT3D echo are accurate and reproducible. This technique expands the use of ultrasound for the noninvasive evaluation of cardiac patients and provides a new tool for the investigational study of cardiovascular disease. ©1999 by Excerpta Medica, Inc.

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In different forms of cardiac disease, left ventricular (LV) volumes constitute an important prognostic indicator, and their measurements thus determine patient management.[1–5] Although several methods can be used to assess LV volumes, most are limited by their invasiveness, cost, or lack of repeatability. The use of 2-dimensional echocardiography for LV volume measurements relies on geometric assumptions which may be inaccurate in diseased ventricles.[6,7] Three-dimensional echocardiography (RT3D echo) has potential advantages because it does not require assumptions of uniform LV geometry.[8–14] Until recently, the technique involved reconstruction of 2-dimensional images acquired over several cardiac cycles,[15,16] a method that has found limited applications for routine clinical use. RT3D echo is a new technique capable of acquiring and simultaneously displaying volumetric cardiac images without electrocardiographic or respiratory gating. This study was designed to develop and validate a method for rapid LV volume calculations with RT3D echo and to determine its usefulness in cardiac patients.

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Address for reprints: Julio A. Panza, MD, National Institutes of Health, Building 10, Room 7B-15, Bethesda, Maryland 20892. E-mail: panzaj@nih.gov.

METHODS

RT3D echo imaging: The method of RT3D echo imaging was first developed in the Center for Emerging Cardiovascular Technologies at Duke University[17,18] and is based on the use of a 2-dimensional phased-array transducer. These 2-dimensional arrays consist of a 43 × 43 element matrix with elements measuring 0.3 × 0.3 mm. For the present studies, a 14-mm array was used with a center frequency of 2.5 MHz (Volumetrics Medical Imaging, model 1, Durham, North Carolina). Figure 1 shows a 2-dimensional array and the pyramidal shaped volume scanned by this array. Scanning in azimuth and elevation are achieved electronically, and 16-to-1 parallel processing is used to increase the scanning speed. Due to the parallelisms in receive, the 64° × 64° pyramidal volume can be scanned at rates of 18 to 40 volumes/s depending on the depth of the scan. For a typical maximum range of 16 cm, the volume rate is 20/s. The RT3D echo system permits the simultaneous display of multiple sectional planes through the scanned volume. These planes include the traditional B-mode planes (origin at the transducer force), C-mode planes (parallel to the transducer force), and inclined C-scans (Figure 1). The position of these planes are under operator control and the thickness of C-scans or inclined planes may be varied from 0.3 to 6.0 mm. Up to 6 seconds of volumetric scan data are stored on a continuous basis. At the cessation of live scanning, a

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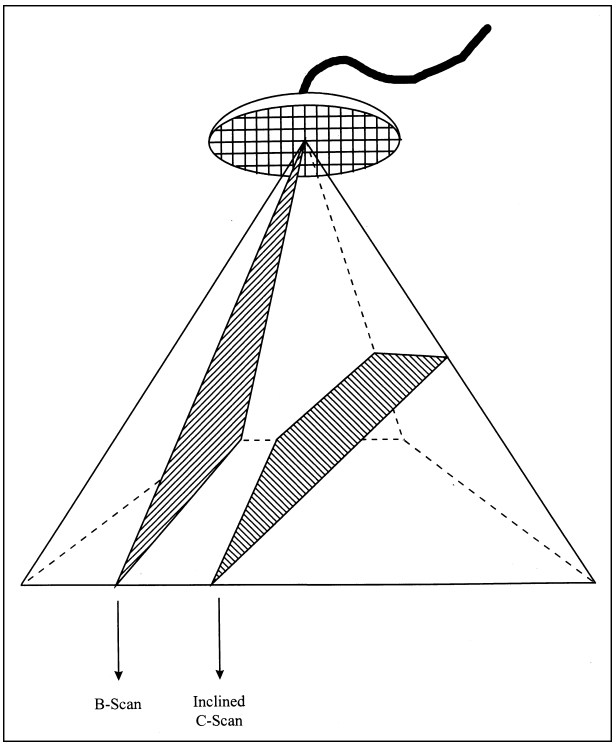

FIGURE 1. Two-dimensional array and pyramidal scan volume for RT3D echo, showing a steerable B-scan plane in the volume and an arbitrarily positionable inclined C-scan.

cine loop feature allows assessment of cardiac anatomy on a single or multiple beat basis. All image plane manipulations available during live scanning are also implemented during cine loop playback, thus permitting the simultaneous display of multiple images positioned anywhere within the scanned volume. Manual tracing on the C-scan images has permitted the accurate determination of right ventricular stroke volume in animal studies.[19]

Study protocol: Twenty-five subjects were enrolled in a prospective study approved by the National Heart, Lung, and Blood Institute Institutional Review Board (NIH protocol # 98-H-0016). Each subject underwent magnetic resonance imaging (MRI) and RT3D echo examinations on the same day in random sequence. Each subject also had a 12-lead electrocardiogram and a routine 2-dimensional echocardiogram recorded to determine the presence or absence of structural heart disease. Only subjects with endocardial borders adequate for measurement of LV volumes were included in this study. All participants gave written informed consent for all procedures. There were 4 normal volunteers and 21 cardiac patients (16 men and 9 women; mean age 46 $\pm$ 14 years). Cardiac diagnoses included ventricular septal defect (2 patients), ischemic cardiomyopathy (2 patients), hypertrophic cardiomyopathy (7 patients), and aortic regurgitation (10 patients). Subjects were excluded from the study if they had a history of atrial fibrillation, unstable angina, or a recent myocardial infarction. Other specific contraindications relative to MRI included pacemaker implant, aneurysm clip, neural stimulator, ear implant, or any metallic foreign body.

MRI scans were performed on a 1.5T scanner with enhanced gradient subsystems (General Electrics Horizon, Waukesha, Wisconsin). The left ventricle was imaged using a prospectively gated, retrospectively sorted cine gradient echo sequence that captures the entire cardiac cycle within a breath hold.[20,21] After obtaining localizer scans, the left ventricle was imaged in multiple parallel short-axis views from the mitral annulus to the apex. The slice thickness was 6 mm without separation, which resulted in 13 to 20 short-axis imaging planes for each subject. Each short-axis slice was acquired on a separate breath hold equivalent to 16 heart beats. The field of view was 36 $\times$ 24 cm, with an image matrix of 256 $\times$ 160 and a 0.75 acquisition. The spatial resolution of the images is approximately 1.4 $\times$ 1.5 mm/pixel. The temporal resolution of images was nominally 72 ms, and at least 20 images were reconstructed across the cardiac cycle. The echo time was 6.0 ms, the repetition time was 11.9 ms. Electrocardiographic gating was provided by an optical ECG device (Magnetic Resonance Equipment, Bay Shore, New York).

RT3D echo images were acquired with the subject in the left lateral decubitus position and the transducer placed at the cardiac apex. The gain and depth controls, as well as the transducer position, were adjusted to optimize the volumetric image so that the entire LV cavity could be visualized from the simultaneously displayed 4- and 2-chamber views. Two to 4 imaging loops containing 32 frames were obtained in each subject. Using the electrocardiographic signal, each loop was subsequently trimmed to encompass an entire cardiac cycle. The highest quality imaging loop was then selected for inclusion in the study and stored on optical disks for subsequent analysis.

Volume calculation by MRI: MRI images were analyzed by 2 independent observers unaware of the measurements obtained by RT3D echo. LV end-diastolic and end-systolic images were selected by identifying the frames showing the largest and smallest LV cavity size, respectively. LV volumes were determined at end-systole and end-diastole by manual planimetry of images on an independent workstation. The LV cavity length was measured on 4- and 2-chamber views during end-diastole and end-systole to ensure that an adequate number of short-axis images were included in the analysis. The endocardial border of LV short-axis images were traced and excluded trabeculations and papillary muscles from the blood pool. Endocardial volumes were summed on a slice-by-slice basis and totaled for estimates of volume that require no geometric assumptions.[22,23] The custom software for volume measurements was calibrated with water-filled phantoms ranging from 7.5 to 465 ml. The correlation between water volume versus MRI imaged planimetry volume was $y = 1.004x - 1.496$; $r = 0.99$; SEE 5.8 ml. The interobserver variability of LV volumes in humans was described by the linear regression $y = 1.06x + 3.79$; $r = 0.99$; SEE 9.5 ml.

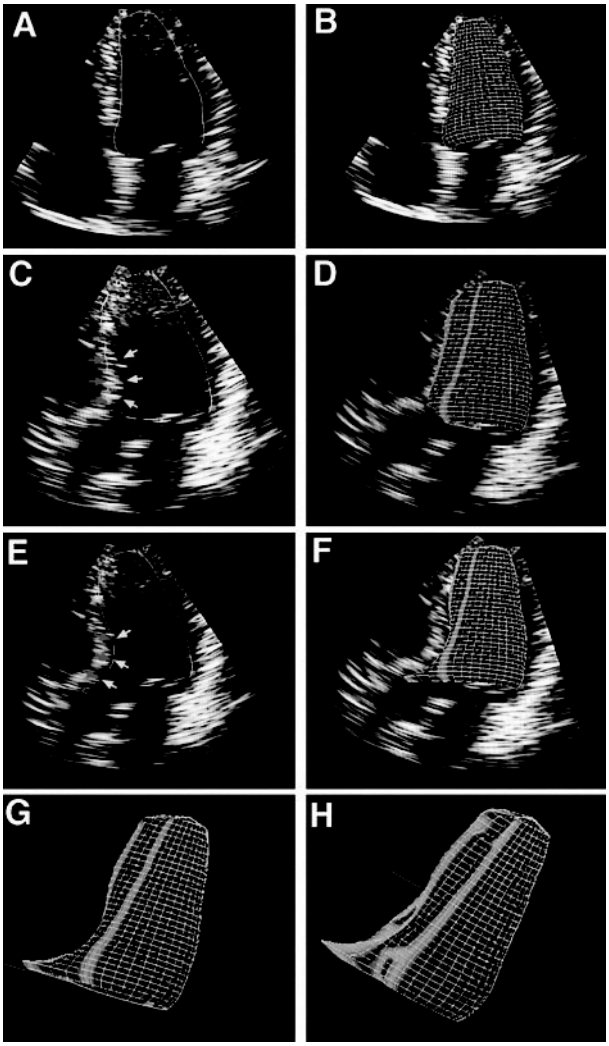

FIGURE 2. Measurement of LV volumes from RT3D echo images using an interactive-aided manual tracing algorithm. After identification of the appropriate (end-diastolic or end-systolic) frame, a coordinate system is established by defining the apex, base, and midventricular endocardium of the left ventricle. The base point establishes the origin of the coordinate system; the apex establishes the direction of the z axis and the scale of the coordinate system. In this illustration, the RT3D echo data are first presented in a slice plane equivalent to the 4-chamber view of a conventional 2-dimensional echocardiographic examination *(A and B)*. The LV endocardium is traced manually with immediate calculation of the corresponding volume. The system allows the traced ventricular surface to be viewed relative to the tomographic slice *(A)*, and also provides a rendered view to allow the tomographic slice to be examined relative to the traced surface *(B)*. After the manual tracing of the LV endocardium is completed in 1 plane, the entire 3-dimensional image can be examined to ascertain proper matching between the computer-generated tracing and the LV endocardium in all planes. *Panel C* shows an instance in which the tracing *(red arrows)* did not match the LV endocardium at the outflow tract level *(yellow arrows)*; this would result in overestimation of the LV volume from the rendered cast shown in *panel D*. The tracing can then be manually adjusted to track the LV endocardium *(E)* with simultaneous automatic correction of the rendered cast (note how the cast follows the contour of the LV outflow tract in *panel F*) and more accurate assessment of LV volume. This manual correction can be performed in any plane and region of the left ventricle as the examiner deems necessary. The finally rendered cast can be examined from different angles *(panels G and H)*; the *blue-shaded areas* on the cast represent regions where manual correction of the tracing was performed. The entire process of calculating both end-diastolic and end-systolic volumes takes approximately 5 minutes. In the slice view *(panels A, C, and E)*, the tomographic slice is always perpendicular to the viewing direction and the traced surface is presented as a contour within the given slice. In the rendered view *(panels B, D, and F)*, the slice is imbedded within the traced ventricular surface and orthographically projected based on a given viewing direction. These views provide 2 unique perspectives on how the geometry of the traced ventricular surface is changing as it is being drawn, and allows the examiner to monitor the development of the traced surface both for a particular LV region and for the entire left ventricle.

Volume calculation by RT3D echo: RT3D echo images were analyzed by 2 independent observers unaware of the measurements obtained with MRI. In addition, each volume measurement was repeated at least 1 week apart by 1 observer to allow subsequent assessment of intraobserver variability. Volumetric images saved into optical disks were transferred to a separate workstation (Silicon Graphics, Inc., Mountain View, California) capable of high-resolution, 3-dimensional volume rendering. LV end-diastolic and end-systolic images were selected by identifying the volumetric frames showing the largest and smallest LV cavity size, respectively. LV volume measurements were determined by an interactive manual tracing technique in which the endocardial border is traced in the apical B-mode images using an algorithm that incorporates the geometric characteristics of the left ventricle.[24] In our experience, measurement of a single LV volume with this software takes approximately 2 to 3 minutes. This method is described in detail in Figure 2 and its corresponding legend.

Statistical analysis: Data are presented as mean ± SD. Because LV end-diastolic and end-systolic volumes in each subject were assessed independently of each other, analysis was initially performed for all LV volumes and then for end-diastolic and end-systolic measurements separately. Two means were compared by paired Student's *t* test. Relations between 2 variables were assessed by means of Pearson's correlation coefficient and by linear regression analysis. The method of Bland and Altman[25] was used to assess agreement between 2 measurements.

RESULTS

Both MRI and RT3D echo studies were completed in each subject within 4 hours. Eleven subjects underwent MRI examination before RT3D echo, whereas the remaining 14 subjects underwent RT3D echo examination first. The average heart rate during the MRI acquisition was significantly lower than that recorded at the time of the RT3D echo examination (62 ± 11 vs 79 ± 16 beats/min, respectively; $p = 0.0001$), and there was no significant correlation between heart rate values measured during the performance of the 2 studies ($r = 0.20$; $p = 0.34$).

LV volume measurements ranged from 25 to 371 ml for MRI and from 24 to 339 ml for RT3D echo. LV volume measurements obtained with MRI were sig-

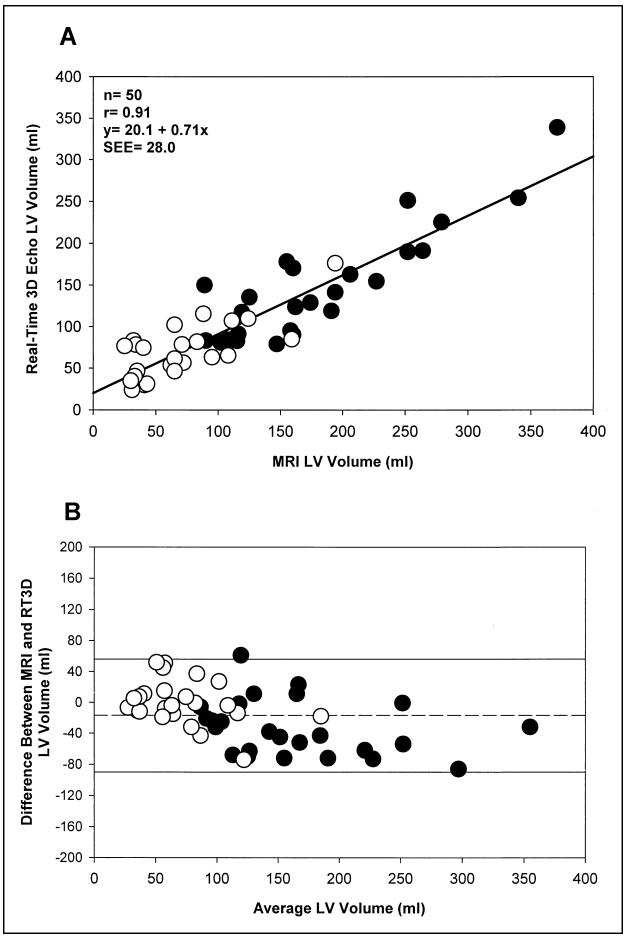

FIGURE 3. Relation between MRI and RT3D echo measurements of LV end-diastolic *(filled circles)* and end-systolic *(open circles)* volumes measured in 25 subjects. *Panel A* shows the correlation between measurements obtained with the 2 techniques. *Panel B* shows the Bland and Altman plot of the difference between MRI and RT3D echo LV volumes as a function of the average calculated volumes[25]; values above the *zero line* represent instances in which the RT3D echo volume was greater than the MRI volume; the *dashed and solid lines* indicate mean ± 2 SDs of the difference, respectively.

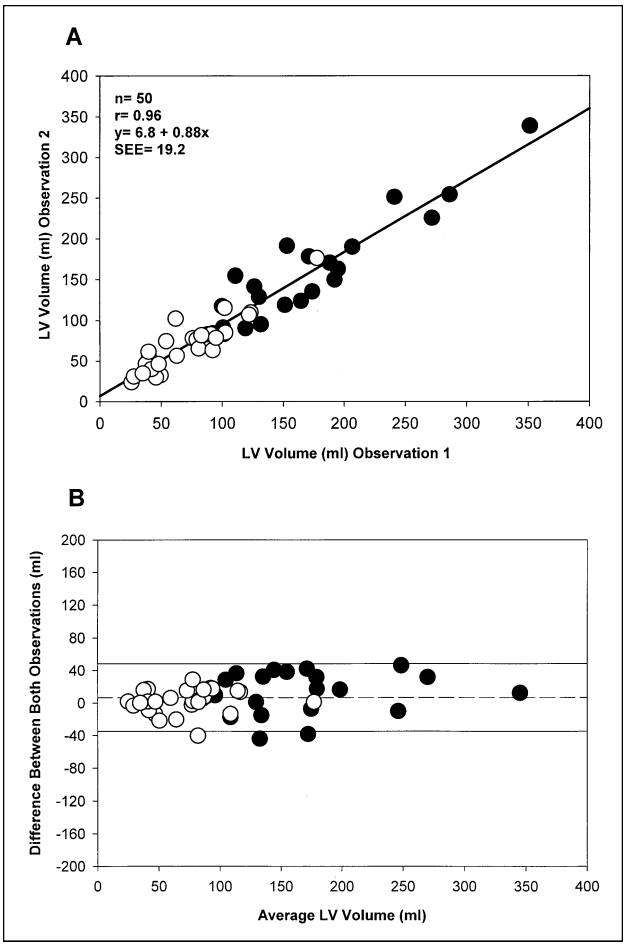

FIGURE 4. Intraobserver variability for RT3D echo measurements of LV end-diastolic *(filled circles)* and end-systolic *(open circles)* volumes obtained in 25 subjects. *Panel A* shows the correlation between 2 measurements obtained by the same observer. *Panel B* shows the Bland and Altman plot of the difference between both measurements as a function of the average measurements[25]; the *dashed and solid lines* indicate mean ± 2 SDs of the difference, respectively.

nificantly greater than those obtained with RT3D echo (126 ± 83 vs 110 ± 65 ml, respectively; p = 0.002; mean difference 17 ± 36). This difference was observed with LV end-diastolic volumes (182 ± 76 ml with MRI vs 149 ± 66 ml with RT3D echo; p <0.0002), but not with LV end-systolic volumes (70 ± 43 ml with MRI vs 70 ± 35 ml with RT3D echo; p = 0.93). A statistically significant correlation was observed between the differences in heart rate recorded during the performance of the 2 studies and the differences in calculated LV volumes with the 2 techniques (r = −0.59; p <0.002). Further, in the 6 subjects whose heart rates during both examinations were within 5 beats, there was a stronger correlation (r = 0.96 vs r = 0.91) and a significantly smaller difference between MRI and RT3D echo volumes (6 ± 19 vs −24 ± 38 ml; p <0.0001) than between those in the remaining 19 subjects with greater differences in heart rates during both examinations.

A strong correlation was observed between LV volume measurements from MRI and from RT3D echo (r = 0.91, mean difference 16 ± 36 ml; Figure 3). The correlation was slightly stronger for end-diastolic than for end-systolic volumes (r values = 0.88 and 0.82, respectively). Both for end-diastolic and for end-systolic volumes, a relation was found between the calculated volumes and the difference in the measurements with MRI and RT3D echo, so that the larger LV volumes were those that showed the greater differences in measurements between the 2 techniques (r = 0.65; Figure 3B). A strong correlation between the MRI and RT3D echo was also observed for calculated stroke volume measurements (r = 0.84), but was less significant for ejection fraction (r = 0.72).

There was a high index of intraobserver (r = 0.96, mean difference 6 ± 17 ml; Figure 4) as well as interobserver (r = 0.98, mean difference 3 ± 15 ml; Figure 5) agreement for the RT3D echo-derived LV volume measurements.

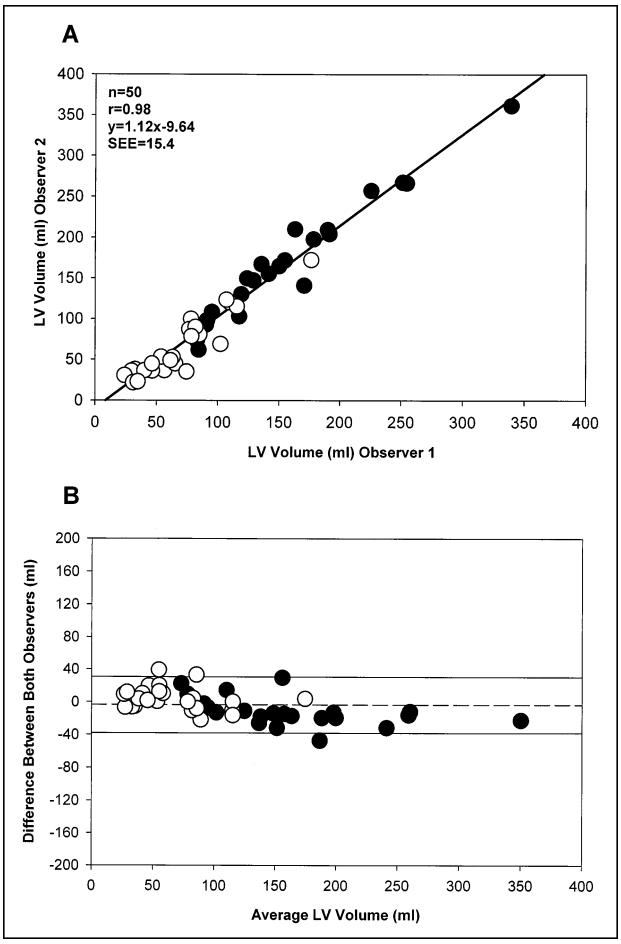

FIGURE 5. Interobserver variability for RT3D echo measurements of LV end-diastolic *(filled circles)* and end-systolic *(open circles)* volumes obtained in 25 subjects. *Panel A* shows the correlation between measurements obtained by 2 different observers. *Panel B* shows the Bland and Altman plot of the difference between both measurements as a function of the average measurements[25]; the *dashed and solid lines* indicate mean ± 2 SDs of the difference, respectively.

DISCUSSION

Findings in the present study demonstrate that RT3D echo, a novel technique capable of providing noninvasive evaluation of cardiac anatomy in real time, is accurate and reproducible for the quantitative assessment of LV volumes. Thus, in a group of patients with different forms of cardiac disease who underwent MRI and RT3D echo examinations on the same day, a strong correlation was observed between the measurements of LV volumes provided by the 2 techniques. Further, analysis of intra- and interobserver variability showed strong indexes of agreement, indicating that measurements of LV volumes obtained with RT3D echo are highly reproducible.

RT3D echo may represent a significant step forward for the evaluation of patients with heart disease. This technique shares the advantages of conventional cardiac ultrasound, in that it is completely noninvasive, provides on-line assessment of images in real time, and allows image acquisition with the use of a hand-held transducer connected to a portable machine. In addition, RT3D echo offers the unique ability to visualize all regions of the left ventricle in a single heart beat. Whereas evaluation of LV volumes from 2-dimensional images requires assumption of LV geometry, RT3D echo measurements are independent of LV shape, and thus may be particularly helpful in patients with asymmetric hypertrophy, regional wall motion abnormalities, and aneurysms, in whom quantitative assessment of volumes is more clinically relevant.

In the present study, measurements of LV volumes from RT3D echo images were obtained on a separate workstation using customized software. This software was developed to provide rapid volume calculations taking full advantage of the acquired volumetric image. The time required for calculation of LV end-diastolic and end-systolic volumes (and therefore ejection fraction) is approximately 5 minutes, and thus similar to that needed to calculate ejection fraction using radionuclide ventriculography. Although the system currently requires relatively expensive hardware capable of handling volumetric images, the rapid developments in computer technology and reduction in costs should make this system available to most institutions in the near future.

In our study, we found that, despite the strong overall correlation between MRI and RT3D echo, there were important discrepancies in the calculation of LV volumes in certain patients. We cannot directly determine whether the larger volumes measured with MRI were due to overestimation by this technique or to underestimation by RT3D echo. This limitation is common to all studies of in vivo measurements of cardiac volumes, for which no true "gold standard" is available. It is possible that those differences were a reflection of lesser accuracy of RT3D echo than with MRI owing to poorer image resolution, weaknesses in the methodology for volume measurements, or both. However, these discrepancies may have been partially due to actual changes in LV volumes occurring between the 2 examinations. Thus, despite our attempt to perform both studies in random sequence, and as close in time to each other as possible, we observed a significantly lower heart rate during MRI acquisition than during RT3D echo examination. Autonomic changes induced by increasing right atrial filling during breath holding may explain the surprisingly lower heart rate during MRI, which, in turn, may account for the larger cardiac volumes recorded with this technique. The relation observed between the differences in heart rate and the differences in measured LV volumes lends further credence to this concept, as do the stronger correlation and smaller differences in LV volume measurements in the subset of patients whose heart rate differences between the 2 examinations were within 5 beats.

Compared with currently available 2-dimensional echocardiography machines, the RT3D echo system used in our study has certain important limitations. First, the RT3D echo system has lower image resolution that limits its use in patients with suboptimal ultrasound window. For this reason, only patients with

adequate images were included in the present study. The use of ultrasound contrast agents that opacify the LV cavity may expand the use of this technique to patients with suboptimal images. Second, the RT3D echo system provides lower temporal resolution. The resulting relatively slow frame rate could be a source of error in LV volume measurements and may partly explain some of the discrepancy observed with MRI measurements in our study. Finally, the RT3D echo examination is limited to a 64° pyramidal volume as opposed to the 90° sector angle provided by conventional 2-dimensional echocardiography, and therefore does not allow a simultaneous assessment of the left and right ventricles in patients with enlarged cardiac chambers. Further technologic developments are necessary for a more comprehensive evaluation of cardiac patients with RT3D echo.

In conclusion, results of the present study indicate that LV volume measurements from images obtained with RT3D echo are accurate and reproducible. This novel technique expands the use of ultrasound for the noninvasive assessment of patients with heart conditions and provides a new tool for the investigational study of cardiovascular disease.

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